Movement Disorders
CLINICAL PRACTICE
REVIEW

Functional Movement Disorders and Placebo: A Brief Review of the Placebo Effect in Movement Disorders and Ethical Considerations for Placebo Therapy

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Abstract: Background: Functional movement disorders are common and disabling neurologic conditions. Patients with functional neurologic disorders represent a large proportion of neurology clinic referrals, and limited availability of subspecialty care creates a considerable burden for the healthcare system. These conditions are currently treated with a combination of physical therapy and cognitive behavioral therapy, with variable success.
Methods: We searched the Medline database for studies on the epidemiology and physiology of functional movement disorders, as well as those on the placebo effect in movement disorders. We reviewed and summarized the literature on these topics and explored ethical issues concerning the administration of placebos to patients with functional movement disorders.
Results: Studies of placebos, particularly in patients with movement disorders, have shown that these "inert" agents can provide demonstrable neurophysiologic benefits, even in open-label studies. Physician surveys have shown that many administer placebos for diagnostic and therapeutic purposes, although there are ethical concerns about this practice. We used a principle-based approach and reviewed ethical arguments for (justice and beneficence) and against (non-maleficence and autonomy) the use of placebos in functional movement disorders. In this context, we argue for the importance of the therapeutic alliance in preserving patient autonomy while exploring the potential benefits of placebo therapy.
Conclusions: An ethical argument is presented in support of nondeceptive clinical placebo use for the treatment of functional movement disorders. Patient and clinician attitudes regarding the use of placebos should be investigated before placebo-therapy trials are conducted.

Functional Movement Disorders

Definition, Epidemiology, and Impact

Functional neurologic disorders (FNDs) have been known by various names, including "psychogenic," "nonorganic," and "hysterical" disorders.[1] Patients present with impaired movement control or abnormal movements that are not fully explained by a known organic (biologically based) illness and that have examination findings not present in conditions with a known or suspected pathophysiologic mechanism. These symptoms are experienced by the patient as involuntary (in contrast to malingering). Although the terminology for these disorders is debated by experts, their impact on patients and on the healthcare system is unquestioned.

FNDs are among the most common conditions encountered in clinical practice, accounting for 16% of patients referred to

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neurology clinics in a large United Kingdom study of nearly 4000 new patients.[2] Functional movement disorders (FMDs) may constitute more than half of these cases.[3,4] FMDs may have phenotypic similarities to hypo- and hyperkinetic movement disorders (including tremor, dystonia, myoclonus, gait disorders, and parkinsonism), but possess key distinguishing characteristics on examination that enable a clinical diagnosis.[5,6] Depending on the case definition and clinical setting, FMD prevalence ranges from 2% to 20% of patients seen in movement disorder clinics.[7] These conditions are not only prevalent, but also highly morbid, with patients reporting levels of disability and quality-of-life impairment similar to those of patients with Parkinson disease (PD).[8] One study showed that neurology outpatients with symptoms unexplained by organic disease experience greater disability and distress than those with medically explained symptoms.[9] The prevalence of and disability associated with these conditions result in substantial expense. A decades-old estimation of the annual cost for the care of patients with somatoform disorders (including FMDs) in the United States was $20 billion, which included redundant diagnostic testing and morbidity from unnecessary medications and procedures.[10,11]

Physiology of Functional Movement Disorders

The pathophysiology underlying FMDs and other FNDs is poorly understood, but progress in characterizing these conditions has been made during the past decade. What has been learned about the role of impaired sense of agency and other possible contributors to the development and maintenance of these disorders is germane to ethical discussions regarding this unique population. In patients with FMDs, movements that are similar or identical in appearance to volitional movements are perceived as involuntary by the individual.[12] The experience of voluntary motion depends on both the perception of one's body as one's own (body ownership) and the sense of authorship of movements (agency).[13] It has been hypothesized that the basis of FMDs is a deficiency in self-recognition of movement and thus an impairment in body agency and/or sense of body ownership.[14] A neurobiological framework was proposed to explain functional motor and sensory symptoms on the basis of hierarchical Bayesian models of brain functioning, assuming an emphasis on minimizing prediction errors and unexpected sensory inputs.[15] In this model, interaction between previous expectations and sensory data generates the subjective perception of movement. The proposed abnormality in functional disorders involves an abnormal belief or expectation that is emphasized and reinforced by top-down attentional processes. The role of beliefs and abnormally increased attention in the generation of functional symptoms is supported by the clinical characteristics of FMDs (distractibility, relief of symptoms with non-physiologic maneuvers). Pathologically high levels of precision regarding sensory and motor predictions result in patients' misinterpretation of movements as involuntary.[15]

Studies using several experimental modalities have suggested an impairment in the sense of agency (SA) in patients with FMDs. Functional magnetic resonance imaging (fMRI) studies have shown decreased functional connectivity between the right temporoparietal junction (a critical region in the SA network) and sensorimotor regions in patients with FMDs compared to healthy controls.[16–18] In another fMRI study in which a virtual reality paradigm was used to modulate SA for a motor control task in healthy control patients and those with FMD, the FMD group reported greater variability in their perceived level of control, associated with selective disruption of the SA network.[19] These findings have led to interest in the use of fMRI findings as a biomarker for functional conditions. A recent study of a small group of patients with FMDs and functional weakness (23 patients, 25 controls) showed that resting-state fMRI had a sensitivity and specificity of 60% and 70%, respectively, for distinguishing patients with FMD from controls.[20] The greatest functional imaging differences were similar to those reported in other studies, including decreased connectivity of the right temporoparietal junction and increased connectivity of the right caudate and left amygdala (discussed later) in patients with FMDs.[20]

SA has also been examined using action-effect binding tasks. Action-effect (also called temporal or intentional) binding studies use an experimental paradigm linking voluntary actions to perceivable effects; the phenomenon of action-effect binding is considered a measure of the voluntariness of actions. Patients with FMD and symptoms associated with psychological factors had less action-effect binding compared with voluntary controls, suggesting reduced SA in these individuals.[21] Similarly, when patients with functional tremor were asked to estimate the timing of their intention to initiate movement, their estimate of intent was much closer to the perceived onset of the action (and, in fact, not significantly different than the timing of the action), again suggesting an impairment in perception of volition.[22] SA has also been studied with electrophysiology by examining sensory attenuation. When movements are self-generated, there is a reduction in the intensity of consequent sensation (e.g., perceived touch) compared with externally generated movements, resulting in a different subjective sensory experience.[23] This normal phenomenon is known as sensory attenuation and can be measured experimentally by examining sensory evoked potentials, which are typically suppressed around the onset of volitional movements.[24] Patients with FMDs do not display the expected sensory attenuation at the onset of voluntary movements compared with healthy controls, thus showing an abnormality in a component of voluntary motion perception, which may be linked to impaired SA.[25,26] Individuals with FMDs are unable to improve motor performance in predictable conditions.[27] This may be related to the finding that those with FMDs demonstrate abnormal maintenance of beta power and failure of beta lateralization on EEG prior to the performance of a motor task, suggesting an impairment in movement prediction.[28] The power in the beta band on EEG normally suppresses and lateralizes before voluntary movement, and these changes are more pronounced when the movement is highly predicted.[29]

In addition to physiologic changes associated with SA, other differences have been demonstrated in those with functional

conditions compared with healthy controls. Hyperactivity of the limbic system has been implicated in the pathophysiology of conversion disorder, and studies have consistently shown increased activity of the amygdala in patients with FNDs.[18,20,30,31] For example, patients with FMDs had increased functional connectivity between the right amygdala and right supplementary motor area while viewing happy or fearful stimuli compared with healthy controls; additionally, an overall pattern of increased amygdala activation with impaired habituation (decrease in response to a stimulus with repeated exposures) for emotional stimuli was observed in patients with conversion disorder.[30,31] Changes in the caudate nucleus may also contribute to effective network changes seen in FMDs, with evidence of increased connectivity between the right caudate and amygdala observed in a recent resting-state fMRI study.[20]

Cognitive biases related to processing of novel information may also be present in patients with FMDs. In a probabilistic reasoning task, patients with FMDs showed a tendency to base their decisions on less sensory information ("jump to conclusions"), and were swayed disproportionately by new sensory evidence compared with healthy controls, regardless of its conflict with previous experience.[32] The authors speculate that this may have relevance to how patients process novel sensory data during physical stressors, which seem to precipitate FMDs in some individuals.[32] Indeed, patients commonly report physical trauma shortly before the onset of FMD symptoms.[33]

Psychological factors and previous trauma are critical to the pathogenesis of FMDs in certain patients. Compared with healthy volunteers and patients with organic focal dystonia, those with FMDs had higher rates of childhood trauma (emotional and physical), greater number of previous traumatic events, and increased fear associated with traumatic episodes.[34] There is also high comorbidity of psychiatric conditions in patients with FMDs. One study using qualitative psychiatric interviews identified current or lifetime psychiatric disorders in 28 of 36 patients, with active conditions in 22 of 36 patients (most commonly anxiety, depression, and/or somatization disorder).[35] In an outcomes study of patients with FMD with a mean of three years of follow-up, an Axis I psychiatric diagnosis was made in 95% of the 42 participants who completed the study.[36] The most common diagnoses were depression and anxiety disorders, and there was also a high prevalence of personality disorders.[36]

An Unmet Need

Despite their high prevalence, FMDs remain challenging to diagnose, and treatment options are limited and poorly studied. The cornerstones of current therapy involve identification and treatment of any underlying psychiatric condition, cognitive behavioral therapy, and physical therapy.[37] The success of this approach is variable, with many patients remaining refractory to treatment.[38,39] A systematic review of 24 studies examining outcomes in more than 2000 patients with functional motor symptoms showed a poor prognosis for these individuals, with 40% experiencing the same or worse symptoms after a mean of seven years of follow-up.[40] Outcomes in patients with functional dystonia or tremor were poorer (symptoms in 66% to 69% were the same or worse at follow-up) than those with functional weakness.[40] A prospective study of 88 patients with FMDs showed persistence of abnormal movements in more than 90% of patients after a mean of three years of follow-up.[36] There are substantial barriers to care for these patients, including limited access to physicians and therapists experienced in the treatment of FMDs and limited availability of insurance coverage for inpatient admission, counseling, and adjunctive treatments (e.g., biofeedback). It is clear that additional treatments for these common and debilitating disorders are needed. Placebos represent a powerful, but controversial, tool that is often used for diagnosis and treatment of functional conditions.

Placebos in Movement Disorders

Defining Placebo, Nocebo, and Lessebo

Traditionally, placebos are defined as physiologically inert substances. A placebo treatment is an intervention that lacks specific pharmacologic or physiologic efficacy for a patient's condition.[41] Placebo effects refer to subjective and objective benefits observed with placebo administration that cannot be attributed to a direct effect of the treatment.[42] These effects are ubiquitous across diseases, patient populations, and experimental paradigms, making them a key consideration in the design of clinical trials. Although the power of placebo effects has been recognized for centuries, only in the past several decades have studies emerged seeking to understand the mechanisms underlying the placebo response. Placebos have often been categorized as "pure" or "impure." Pure placebos refer to the most classic definition of a physiologically inert substance, such as a sugar pill or saline injection, presented to the patient as a medication.[43] Impure placebos are substances that may be biologically active for some conditions, but are probably not useful for the condition for which they are given (e.g., vitamins for unproven indications or antibiotics for viral infections).[43,44] Impure placebos represents the most common form used by modern practitioners.

Patient expectations may also influence treatment outcomes in other, less favorable ways. The nocebo response refers to the opposite of the placebo response, whereby the patient's negative perceptions or expectations lead to clinical worsening with treatment.[45] The term "lessebo" has been used to describe a reduction in the magnitude of the therapeutic effect in an active treatment group in a clinical trial because of the participants' knowledge that they may be receiving a placebo treatment.[46] Both nocebo and lessebo effects have been reported in patients with PD in the context of clinical research.[46,47]

Unfortunately, to date, no studies focusing on the placebo response or its physiology in FMDs have been published, to the authors' knowledge. We will therefore briefly discuss what is known about placebo effects in other movement disorders (mainly PD).

Physiology of Placebo Effects in Movement Disorders

Two main mechanisms have been emphasized in the study of placebo effects: expectation (anticipation of a therapeutic benefit) and learning (activation of reward pathways based on previous therapeutic experiences).[48] Both can be illustrated using the example of PD.

The placebo response in PD is mediated by the release of endogenous dopamine.[49] Positron emission tomography studies show that dopamine receptors are activated in the dorsal and ventral striatum when a placebo is administered to patients with PD.[49–51] Dopaminergic activation in the ventral striatum (specifically, in the nucleus accumbens) is related to the expectation of reward, because this is observed regardless of whether the individual experiences subjective benefit from the placebo treatment.[50] Additionally, intraoperative recordings from single neurons during electrode implantation for deep brain stimulation (DBS) surgery in patients with PD have shown changes in firing rates with placebo administration. There is a decrease in the firing rate of neurons in the subthalamic nucleus and substantia nigra pars reticulata, along with a disappearance of bursting activity in the subthalamic nucleus with placebo administration.[52,53] The firing rates of neurons in the ventral anterior thalamus and anterior ventral lateral thalamic nuclei increase when placebo treatment is administered.[53,54]

Intraoperative single-neuron recordings have also illustrated the importance of learning in the generation of the placebo response. First-time administration of placebo produced no significant changes in wrist rigidity or in the firing rate of thalamic neurons, but preconditioning with the dopamine agonist apomorphine produced clinical and electrophysiologic responses in a dose-dependent manner (the greater the number of previous exposures to apomorphine, the greater the magnitude and duration of the placebo response).[55] The influence of previous drug exposure on the placebo response in PD has also been shown in a clinical study that used changes in bradykinesia as the primary endpoint.[56]

Placebo Responses in Other Movement Disorders

Placebo effects are powerful in patients with movement disorders, with most studies focused on patients with PD. A systematic analysis of 858 patients in placebo groups from published medical and surgical trials for PD further characterized the placebo response.[57] Positive placebo response in this review was defined as at least 50% improvement in total Unified Parkinson's Disease Rating Scale motor (UPDRSm) score or a decrease of two or more points on at least two UPDRSm items compared with baseline. The overall rate of positive placebo response was 16% (range, 0% to 55%), and placebo responses occurred during the entire six-month follow-up period.[57] Surgical treatment was associated with increased odds of a positive placebo response.[57] In PD, all domains of motor impairment may improve with placebo administration.[58]

Surgical treatment is more likely to produce a placebo response than nonoperative treatment, with an odds ratio of 4.64 in the systematic analysis described above. The three included surgical trials involved cell transplantation and used burr holes without dural penetration.[57] The use of sham surgery controls in studies of invasive treatments for PD has been at the center of an ethical debate that is beyond the scope of this review.[59] The effect of perceived treatment expense (demonstrated with medical placebo in PD) may influence the placebo response after surgery in these patients.[60] Patients preparing to undergo DBS surgery for PD also have a strong expectation of motor benefit, which may be a contributing factor.[61] The role of expectation and the placebo response have been examined in subthalamic nucleus DBS in several studies, which showed significant differences in motor function depending on disclosure to the patient of whether stimulation was activated or inactivated.[62,63] The placebo response is an important consideration across the spectrum of therapeutic interventions in PD.

There are few studies of placebo responses in other movement disorders. In a longitudinal study of patients with Huntington disease, only behavior showed a significant placebo response, rather than motor or cognitive function.[64] An analysis of 91 control patients in six trials for tic disorders showed a common (19% of patients) but negligible placebo effect.[65] Despite the many studies focused on placebo effects in PD, this has not been a subject of investigation in FMDs.[66]

Use of Placebos in Functional Movement Disorders—Attitudes and Ethical Considerations

Current Attitudes of Physicians and Patients

Surveys of physicians have shown that a significant number (17% to 99% of respondents) use pure (saline injections/sugar pills) or impure (e.g., vitamins for unproven indications) placebos for diagnosis and treatment of patients with various conditions.[67–69] Although many respondents believed that this practice was ethically permissible under certain circumstances, most also reported that they found use of placebos to be problematic for various reasons.[67–69] Most physicians surveyed believe that placebos can have therapeutic effects.[70] Despite the many viewpoints on the ethics of placebo use, there has been little investigation of patients' perspectives on the issue. For example, a small study performed in Sweden suggested that patients' attitudes toward the acceptability of placebos were more positive than those of physicians, and a higher percentage of patient respondents advocated deceptive prescribing of placebos.[71] A recent telephone survey of patients in the United States also showed that most found placebo use acceptable, with potential for benefits and lack of harm the reasons most often provided.[72] Only 20% of

TABLE 1 A principle-based approach to the consideration of placebo use for FMDs.

Principle	Argument for placebo	Argument against placebo
Respect for autonomy	Nondeceptive placebo may be an autonomous choice of the patient	Use of deception may be a violation of autonomy/ informed consent
Non-maleficence	Unlikely to cause substantial physiological harm	Possibility for psychological harm
Beneficence	Potential to benefit the patient who has no other therapeutic options	Potential to eliminate benefit or harm patient when deception is discovered
Justice	Potential to lower overall societal costs related to FMDs; low-cost treatment accessible to more individuals	Potential for use of only placebos (given cost) and underutilization of more expensive therapies

Abbreviations: FMD, functional movement disorder.

853 respondents in this study thought that it was never acceptable for physicians to recommend placebo treatments.[72] Therefore, although data are limited, it seems that most patients surveyed find the use of placebo therapy permissible in certain situations, and that patients report more tolerance of deceptive prescribing than do responding physicians. However, there are multiple ethical principles at play when considering the use of placebos in FMDs.[73] A few main considerations are listed using a principle-based approach in Table 1 and discussed below.

Ethical Arguments in Favor of Placebo Use in Functional Movement Disorders

Justice

FMDs are common neurologic conditions that are often challenging to diagnose and treat. The financial burden related to FMDs is substantial for multiple reasons, including disease prevalence, cost of care, and lost productivity because of high levels of disability.[7] Despite the existence of diagnostic criteria for FMDs, patients often seek multiple opinions regarding the diagnosis and treatment of their symptoms. Numerous diagnostic studies may also be requested. This pursuit may be time-consuming, expensive, and of limited utility in most cases because the criteria for FMD diagnosis are based on the patient's history and examination and are often unaffected by the results of ancillary testing.[5,6,74] The principle of justice—namely, fair distribution of resources—is an important consideration when discussing the ethics of placebo use in FMDs. There are several ways in which one could consider the clinical use of placebos in FMDs to be consistent with the promotion of justice. Use of placebos to facilitate diagnosis and treatment of FMDs may decrease health care costs by reducing unnecessary testing and pursuit of alternative therapies. Additionally, limited availability of subspecialty care is another factor in the discussion of allocation of healthcare resources. As the United States population ages, the shortage of movement disorder neurologists is expected to increase, and placebo use may decrease patients' reliance on these specialists for redundant evaluations of functional symptoms,[75] especially in medically underserved communities.

Beneficence

An argument can be made for beneficence (the promotion of the patient's welfare) from a diagnostic and therapeutic standpoint for placebo use in patients with FMDs. Early descriptions of patients with FMDs include response to placebo as a clinical feature and diagnostic consideration in these disorders.[4] Now that the power of placebo effects has been increasingly recognized in organic disorders such as PD, the utility of placebo response as a diagnostic criterion is dubious. The role of placebos in facilitating diagnosis of functional conditions requires further exploration, as this could still be a useful tool in these sometimes difficult-to-diagnose disorders. This is particularly relevant because it has been consistently shown[4] that delays in diagnosis and initiation of treatment are associated with poorer prognosis in individuals with FMDs.[3,4,39] In our view, the lack of therapeutic options available for patients with FMDs makes beneficence the primary ethical consideration for the use of placebo as a treatment option.

Although the effect of placebo administration in FMDs has not been examined (there have been no randomized placebo-controlled studies for these patients), the placebo response is anecdotally robust in this population, as expected from research in other neurologic disorders. Assuming that symptomatic improvement could be anticipated, the argument has been made that there is a moral obligation to offer placebo therapy for these patients, who are often severely debilitated by their symptoms and may have no other options for relief.[66]

Ethical Arguments Against Placebo Use in Functional Movement Disorders

Non-maleficence

The principle of non-maleficence, or avoidance of harm, could also support the use of pure placebos in FMDs because the physical risk is minimal (aside from sham surgery, which is irrelevant to the care of patients with FMDs). Yet there is a stronger argument based on non-maleficence against the use of placebos. The potential harm from pure placebo use concerns primarily the therapeutic relationship with and erosion of trust in the physician and the broader health care system. Patients with FMDs are already likely

to feel stigmatized within the health care system because of the difficulty of FMD treatment, stigmatization of disorders involving psychological factors, and frequent grouping of these disorders with conditions such as malingering. There is a potential for major harm if a patient discovers that a physician has been using a placebo deceptively, causing the patient to lose trust in the physician and health care system.

Additionally, impure placebos have the potential for adverse physical effects, as well as broader negative consequences (e.g., the use of antibiotics to treat viral infections contributing to antibiotic resistance), and may thus be more problematic than pure placebos. This is pertinent because impure placebos constitute most placebo use in modern clinical practice.

Another criticism based on non-maleficence is that using placebos to treat FMDs as a "quick fix" could result in failure to address the underlying psychological or psychiatric contributors to disease and possibly lead to the medicalization of benign somatic complaints.[44] According to this view, placebos would best be used as an adjunctive therapy and would not replace psychotherapy or physical therapy (if these are indicated). However, approximately one-third of patients with FNDs lack any identifiable psychiatric comorbidity and would thus be unlikely to benefit from psychotherapy.[76]

Autonomy

The principle of autonomy refers to the right of patients to make informed decisions about their care. The strongest ethical argument against the use of placebos in clinical practice concerns deception. Misinformation or lack of transparency about prescribed interventions violates patient autonomy, as well as the ethical (and legal) requirement to obtain informed consent for treatment.[44] Protection of patient autonomy is particularly important in patients with FMDs because an impaired SA likely contributes to the pathophysiology of this disease state. The American Medical Association's Code of Medical Ethics forbids the deceptive use of placebo in clinical practice, as do the British Medical Association's published ethical guidelines.[77,78] The legal implications of this are unclear. However, survey studies suggest that patients may find deceptive placebo use more tolerable than do physicians.[71,72] More importantly, open-label placebo (OLP) studies show that deception may not be necessary for the realization of the benefits of placebo effects. A recent randomized, controlled trial of OLP for chronic low back pain showed an improvement in pain and disability scores after three weeks compared with treatment-as-usual.[79] Similar results were achieved for a randomized study of OLP in irritable bowel syndrome.[80] In fact, a recent meta-analysis of five trials in 260 patients with various conditions (including the two previously mentioned studies) examining OLP compared with no treatment showed a positive effect for OLP therapy, with a significant ($p<0.0001$) and moderate effect size.[81] However, these studies were small, with heterogeneous designs/study populations and short duration of follow-up (14 to 21 days). Therefore, it is unclear whether there is a potential long-term benefit of OLP treatment for FNDs. However, this research suggests that placebos can exert therapeutic effects when administered with the informed consent of the patient. Unlike deceptive placebo use, administration of placebo therapy with informed consent is permissible according to the American Medical Association's Code of Medical Ethics.[77] Of note, other organizations worldwide, including the World Medical Association and the International Code of Medical Ethics, are less explicit, focusing on the appropriate use of placebo in research applications without addressing clinical practice.[82,83]

Model for Implementation

Placebo effects are probably at work, to an extent, in nearly every clinical encounter. In real-world practice, the prescription and administration of therapies cannot be divorced from the psychosocial context and the physician-patient relationship. The interaction between clinician and patient has substantial power to shape the patient's experience (in a positive or negative fashion).[84] The importance of context is shown in multiple studies reporting a decrease in efficacy when treatments are administered covertly rather than openly in patients with various neurological conditions.[85] Annoni and Miller[86] describe a framework for using therapeutic communication (a deliberate manner of communicating with patients) to maximize potential placebo effects when using proven therapies and OLPs. After a discussion of the moral principles of truthfulness, helpfulness, and pragmatism for this approach, they conclude that it is possible to promote positive expectations about the effectiveness of placebo therapy without compromising truthfulness.[86] Similar conclusions about the ethical permissibility of counseling patients about placebo therapy may be reached with a focus on shared decision making in clinical practice.[87] Successful implementation of clinical nondeceptive placebo use calls for educating the patient on the definition and evidence in support of placebo therapy, with transparent disclosure of the intention of treatment and optimistic expectations regarding outcome.

Future Directions, Knowledge Gaps, and Conclusions

Although much remains to be learned about the pathophysiology of FMDs, recent advances have led to the emergence of a plausible biopsychosocial model of these disorders.[15] However, FMDs continue to represent a serious diagnostic challenge across subspecialties and are a severe economic burden on the health care system. Moreover, there is a glaring lack of effective therapies for these disorders, further complicated by lack of patient access to the specialized care required for FMDs. From an ethical standpoint, there seem to be few barriers to nondeceptive administration of placebo treatments for FMDs and other disabling conditions for which there are no effective alternative therapies. This option would need to be honestly and transparently presented to patients in order to respect autonomy and shared decision-making. Additional information about the opinions of patients with FMDs regarding the acceptability of placebo use would be valuable, because this has not been studied in this population. Informed by systematically gathered patient-derived information, an OLP study in patients with FMDs compared with usual care would be the next logical step. Further study

is warranted to clarify the potential role of placebo therapy in the treatment of patients with FMDs.

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Author Roles

1. Research Project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing the First Draft, B. Review and Critique.

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